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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	Group Art Unit: 1632
WEINSTEIN, Bret S.	)	Examiner: Woitach, Joseph T.
Serial No.: 09/884,183	)	
Filed: June 19, 2001	)	
For: Method of Breeding Laboratory Animals to Optimize Tumor Suppression and Tissue Repair Functions in Vivo and Improved Methods for Conducting Experiments and Safety Testing	)	Pasadena, California

TRANSMITTAL LETTER

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450	"EXPRESS MAIL" mailing label number **EV 629344105 US** Date of Deposit **August 31, 2005** I hereby certify that this paper is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 C.F.R. § 1.10 on the date indicated above and is addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 Elaine Porter Elaine Porter

Sir:

In response to the Notification of Non-Compliant Appeal Brief dated August 11, 2005, Applicant hereby submits a revised Appellant's Brief (and two additional copies). Applicant respectfully submits that the revised Appellant's Brief contains all of the items required under 37 CFR 41.37(c). Applicant has added a concise statement of each ground of rejection presented for review pursuant to 37 CFR 41.37(c)(1)(vi) and has removed

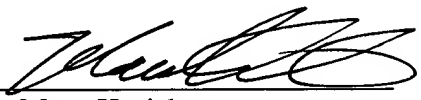
the section entitled "Grouping of Claims." Accordingly, Applicant respectfully requests that the revised Appellant's Brief be entered and considered.

No fee is believed due with this communication. However, the Commissioner is authorized to charge any fee due to Deposit Account No. 19-2090.

Respectfully submitted,

SHELDON & MAK PC

DATED: August 31, 2005

By 

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APPELLANT'S BRIEF

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450	"EXPRESS MAIL" mailing label number **EV 629344105 US** Date of Deposit. **August 31, 2005** I hereby certify that this paper is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 C.F.R. § 1.10 on the date indicated above and is addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 Elaine Porter

Sir:

This is an appeal from the Final Rejection, dated September 23, 2004, of the claims in the above-referenced application.

1. **REAL PARTY IN INTEREST**

The real party in interest is the inventor of the application, Bret Weinstein.

2. RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences presently pending that are known to appellant or appellant's attorney.

3. STATUS OF THE CLAIMS

Claims 5 to 7 are pending in the application. All of the claims have been rejected. The rejections of all of the claims are appealed.

4. STATUS OF AMENDMENTS AFTER FINAL REJECTION

No claim amendments have been made after Final Rejection.

5. SUMMARY OF THE CLAIMED SUBJECT MATTER

The invention relates to the breeding of laboratory animals having a defined range of telomere lengths.[1] A first population of animals comprising cells comprising chromosomes with telomeres of determinable lengths is selected.[2] A statistical distribution of telomere lengths among cells of the animals of said first population is determined.[3] Animals with a desired distribution of telomere lengths are allowed to produce offspring.[4]

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[1] Citations to the application will be in the form "(page:lines)" throughout. *See*, (4:1-6:17)

[2] See, 4:5-6.

[3] See, 4:21-25.

[4] See, 5:5-15.

6. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The grounds of rejection to be reviewed on appeal are whether or not the Examiner properly rejected claims 5 to 7 under 35 U.S.C. §112, first paragraph, as allegedly being unpatentable because the claimed invention is not supported by either a specific or substantial asserted utility, and because one skilled in the art would not know how to use the claimed invention.

7. ARGUMENT

A. Introduction

The Examiner rejected claims 5 to 7 under 35 U.S.C. §112, first paragraph. The Examiner alleges that the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility, and that one skilled in the art would not know how to use the claimed invention. Additionally, the Examiner refers to the previous Office action dated December 18, 2003 in which the Examiner took issue with the assertion in the specification that nuclear transfer could be used to alter telomere length, because the art of nuclear transfer is unpredictable.

The Examiner's rejection pursuant to 35 U.S.C. §112, first paragraph is improper. As the Examiner admits, the Applicant has asserted a utility to provide animal lines with defined telomere length, which is supported by the specification.[5] As explained in the specification, these animal lines can give researchers an accurate picture of the probable risks, costs, hazards and dangers that humans, pets and other species are likely to face when exposed to the agents and procedures being tested on them.[6] The use of laboratory animals in experimentation is well known, and the animals created using the methods of the present invention can be utilized in the same manner as present laboratory animals. One skilled in the art would immediately understand a myriad of specific, substantial and credible uses for

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[5] See, Office Action dated September 23, 2004, page 2.

[6] See, 4:2-5.

laboratory animal lines created using the methods of the present invention, including the duplication of previously performed experiments to obtain more reliable results.

B. The Present Invention Has Credible, Specific, and Substantial Utility

1. The Legal Standard For Utility

35 U.S.C. §112, first paragraph states:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A lack of utility has been equated with a lack of enablement in violation of 35 U.S.C. §112, first paragraph. The examination guidelines for utility are explained in sections 2107-2107.03 of the Manual of Patent Examining Procedure. Section 2107.02 states that even if no statements can be found asserting a specific and substantial utility for the claimed invention in the specification, an invention has a well-established utility if (i) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention, and (ii) the utility is specific, substantial, and credible. "If an invention has a well- established utility, rejections under 35 U.S.C. 101 and 35 U.S.C. 112, first paragraph, based on lack of utility should not be imposed. *In re Folkers*, 344 F.2d 970, 145 USPQ 390 (CCPA 1965)."

As stated in section 2107, "An applicant need only provide one credible assertion of specific and substantial utility for each claimed invention to satisfy the utility requirement." Moreover, the Examiner "must treat as true a statement of fact made by an applicant in relation to an asserted utility, unless countervailing evidence can be provided that shows that one of ordinary skill in the art would have a legitimate basis to doubt the credibility of such a statement."

2. **A Correlation Exists Between Telomere Length And Suitability For Laboratory Experimentation**

As explained in the specification on page 2, line 12 to page 3, lines 22, laboratory mice are only allowed to breed for eight months. Over the last half century this has radically altered the telomeres of lab mice compared to wild mice. The telomeres of lab mice are typically ten times longer than the telomeres of normal mice. As a consequence, lab mice overwhelmingly die of tumors, show few signs of decline with age, have an extraordinary ability to regenerate tissue with age, and have an extraordinary ability to repair damage throughout life.

These differences have led to problems with current lab mice for use in testing drugs, pesticides and other chemical agents and procedures. For example, some substances that have been shown to cause cancer in lab mice, such as saccharin, seem to produce no such effect in humans. Conversely, for example, Seldane (terfenadine), Fen-Phen (fenfluramine, phentermine, dexfenfluramine), and Ritalin (methylphenidate), which are now suspected of doing tissue damage in humans, did not cause enough harm to laboratory animals to raise appropriate safety questions. See also, page 19, lines 3 to page 20, line 6; and page 29, line 21 to page 30, line 5.

Accordingly, as explained on page 4, lines 2 to page 6, line 3, breeders need to breed test animals in such a manner that laboratory tests can give researchers an accurate picture of the probably risks, costs, hazards and dangers that humans, pets and other species are likely to face when exposed to the agents and procedures being tested.

The claims of the present invention are directed to a method of breeding an animal line for experimental use. The Examiner withdrew the rejection pursuant to 35 U.S.C. §101 and admits that the claimed method should result in an animal line with a defined telomere length.[7] An animal line with a defined telomere length has specific and substantial utility in being able to provide a more accurate picture of the probable risks, costs, hazards,

[7] Office Action mailed on September 23, 2004, page 2.

and dangers that humans, pets and other species are likely to face when exposed to the agents and procedures being tested.

Moreover, a range of telomere lengths can be selected for generalized testing. "A range of telomere lengths surrounding an optimal balance point (between tissue repair capacity and tumor suppression effectiveness) would allow simultaneous testing for carcinogenic effects as well as tissue damage and accelerated aging effects."[8] Additionally, "a fixed optimum target for telomere length can be set in order to produce model organisms better suited to illuminate dangers of one of two opposing types: carcinogenic effects, and tissue damage/accelerated aging."[9]

3. **A Correlation Exists Between Telomere Length And Specific Disorders**

As seen from a review of the scientific articles cited in the application by the Applicant there is a correlation between telomere length and specific disorders. Thus, the present invention has substantial and specific utility in teaching a method for creating lines of laboratory animals with specific telomere lengths.

As explained in Telomere Length Predicts Replicative Capacity Of Human Fibroblasts, patients with Hutchinson-Gilford Progeria are born with short telomeres and age rapidly.[10] As seen in Fig. 1, the mean terminal restriction fragment (TRF) length of human skin fibroblasts declines about 1.5 kbp during the life span of a human from about 8.3 kbp to about 6.8 kbp. TRF is considered a good indicator of telomere length. As explained on page 10116 and shown in Fig. 3, telomere length is reduced in Fibroblasts of Hutchinson-Gilford progeria patents compared to those of normal donors.

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[8] 5:22-25.

[9] 5:26-28.

[10] Allsopp, R.C., Vaziri, H., Patterson, C, Goldsteing, S., Younglai, E.V., et al., 1992 Telomere Length Predicts Replicative Capacity Of Human Fibroblasts. Proc. Natl. Acad. Sci. 89, 1014-10118

Additionally, as explained in Telomere Length And Replicative Aging In Human Vascular Tissues, short telomeres in circulatory tissue are associated with atherosclerosis.[11] "Our results show that endothelial cells lose telomeres in vitro as a function of replicative age and that telomere loss, in vivo, is generally greater in those tissues involved in or susceptible to atherogenesis."[12]

Thus, manipulation of the telomere length in laboratory animals is desireable to test drugs and procedures relating to specific diseases, such as Hutchinson-Gilford progeria patients, and such as atherosclerosis. Thus, the present invention has a utility in providing a method for creating such lab animals.

The Applicant has shown specific and substantial utility of the invention in producing laboratory animals that are better for testing the probable risks, costs, hazards, and dangers that humans, pets and other species are likely to face when exposed to the agents and procedures being tested. The Applicant has also shown specific and substantial utility of the invention in producing laboratory animals particularly useful for testing drugs and procedures for specific diseases influenced by telomere length. Accordingly, the utility rejection pursuant to 35 U.S.C. §112, first paragraph should be withdrawn and the claims allowed to issue.

C. One Skilled In The Art Would Know How To Use The Resulting Animal Line.

Animal based experimentation for the efficacy and risks of drugs and procedures is well known in the art. One skilled in the art will immediately recognize that animal lines created pursuant to the method of the present invention can be utilized the same as existing animal lines.

Additionally, animal lines may be created pursuant to the present invention for specific types of testing. For example, a population of laboratory animals with a range of

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[11] Chang, E., Harley, C.B., 1995. Telomere Length And Replicative Aging In Human Vascular Tissues. Proc. Natl. Acad. Sci. 92, 11190-11194.

telomere lengths surrounding an optimal balance point (between tissue repair capacity and tumor supporession effectiveness) can be used for simultaneous testing of carcinogenic effects as well as tissue damage and accelerated aging effects.[13] Also, for example, a population of laboratory animals with a fixed telomere length can be created to test for either carcinogenic effects or tissue damage/accelerated aging effects.[14]

D. **Any Unpredicatability In The Art Should Not Prohibit Allowance Of The Claims Of The Present Invention**

The Examiner's arguments in the Office action mailed on December 18, 2003 that nuclear transfer is an unpredictable art should have no bearing on the allowability of claims 5-7. Claims 5 and 6 do not contain any limitations that necessitate the use of nuclear transfer. Likewise, claim 7 does not require the use of nuclear transfer.

Claim 7 recites the limitation of "altering a telomere length of one or more chromosomes contained in a germ cell of an animal belonging to said first population." However, as explained in the specification, alteration of telomere length can be done using a variety of methods including: enzymatic lengthening of telomeres using the enzyme telomerase, or its equivalent, to lengthen telomeres, transferring of desirable telomeres, or chromosomes containing desirable telomeres, into target cells which will ultimately produce germ-line cells, shortening telomeres via in vitro mitotic cell culture; and via cloning. Not all of these methods require nuclear transfer. The Examiner should not read into a claim, unclaimed results, limitations or embodiments of an invention. See, *Carl Zeis Stiftung v. Renishaw PLC*, 945 F.2d 1173 (Fed. Cir. 1991); *In re Krimmel*, 292 F.2d 948 (CCPA 1961).

Accordingly, because none of the claims require the use of nuclear transfer, any unpredictability of the nuclear transfer art should not prevent allowance of claims 5 to 7 of the present application.

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[12] Id. at 11190.
[13] See, 5:22-25.
[14] See, 5:26-28.

E. **Conclusion**

Claims 5 to 7 are directed to an invention with credible, specific and substantial utility. Specifically, the specification and cited references make clear that the claimed method of creating animal lines would result in an animal line with specific telomere characteristics. The animal line is particularly useful in testing the probable risks, costs, hazards, and dangers that humans, pets and other species are likely to face when exposed to a particular drug or procedure. Additionally, the laboratory animals are useful for testing drugs and procedures for specific diseases influenced by telomere length. One skilled in the art would be able to use laboratory animals created in accordance with the methods of the present invention in existing experimental protocols as well as in specific experiments for carcinogenic effects or tissue damage/accelerated aging effects.

Accordingly, the Examiner's rejection of the claims pursuant to 35 U.S.C. §112, first paragraph should be withdrawn and a notice of allowance is appropriate.

No fee is believed due with this communication. However, the Commissioner is hereby authorized to charge any fees associated with Appellant's Brief, including extensions of time if required, to Deposit Account No. 19-2090.

Respectfully submitted,

SHELDON & MAK PC

DATED: August 31, 2005

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CLAIMS APPENDIX

Claims 1-4 (Canceled)

5. (Original) A method of breeding an animal line for experimental use, comprising:

preselecting a first population of one or more conspecific animal(s) comprising cells comprising chromosomes with telomeres of determinable lengths;

determining a statistical distribution of telomere lengths among cells of the animals of said first population;

permitting animal(s) with a desired distribution of telomere lengths to produce offspring.

6. (Original) The method of Claim 5, further comprising selecting the offspring to produce a second population, such that the statistical distribution of telomere lengths among the animals of said second population is modified compared to the distribution among the animals of said first population, wherein said second population is intended for experimental use.

7. (Original) The method of claim 5, further comprising the step of altering a telomere length of one or more chromosomes contained in a germ cell of an animal belonging to said first population.

Claims 8-20 (Canceled)